

## PENT COOPERATION TREA

From the INTERNATIONAL BUREAU

**PCT**  
**NOTIFICATION OF ELECTION**  
 (PCT Rule 61.2)

BEST AVAILABLE COPY

Date of mailing (day/month/year) 20 April 2001 (20.04.01)	To:  Commissioner US Department of Commerce United States Patent and Trademark Office, PCT 2011 South Clark Place Room CP2/5C24 Arlington, VA 22202 ETATS-UNIS D'AMERIQUE in its capacity as elected Office
International application No. PCT/US00/17864	Applicant's or agent's file reference X-12591
International filing date (day/month/year) 21 July 2000 (21.07.00)	Priority date (day/month/year) 29 July 1999 (29.07.99)
Applicant  BRINER, Karin et al	

## 1. The designated Office is hereby notified of its election made:

in the demand filed with the International Preliminary Examining Authority on:

02 February 2001 (02.02.01)

in a notice effecting later election filed with the International Bureau on:

\_\_\_\_\_

2. The election  was

was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland  Facsimile No.: (41-22) 740.14.35	Authorized officer  S. Mafia  Telephone No.: (41-22) 338.83.38
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# PATENT COOPERATION TREATY

From the

INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

TUCKER, R. Craig  
 ELI LILLY AND COMPANY  
 Lilly Corporate Center  
 Indianapolis, Indiana 46285  
 ETATS-UNIS D'AMERIQUE

**RECEIVED**

MAY 04 2001

ELI LILLY & COMPANY  
 PATENT DIVISION

**PCT**

NOTIFICATION OF TRANSMITTAL OF  
 THE INTERNATIONAL PRELIMINARY  
 EXAMINATION REPORT

(PCT Rule 71.1)

Date of mailing (day/month/year)	25.04.2001
-------------------------------------	------------

Applicant's or agent's file reference  
 X-12591

**IMPORTANT NOTIFICATION**

International application No.  
 PCT/US00/17864

International filing date (day/month/year)  
 21/07/2000

Priority date (day/month/year)  
 29/07/1999

Applicant

ELI LILLY AND COMPANY et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

**4. REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/



European Patent Office  
 D-80298 Munich  
 Tel. +49 89 2399 - 0 Tx: 523656 epmu d  
 Fax: +49 89 2399 - 4465

Authorized officer

Brell, S

Tel. +49 89 2399-7271



**PATENT COOPERATION TREATY**

From the INTERNATIONAL SEARCHING AUTHORITY

**PCT**

To:

ELI LILLY AND COMPANY  
Attn. TITUS, Robert D.  
Lilly Corporate Center  
Indianapolis, Indiana 46285  
UNITED STATES OF AMERICA

**NOTIFICATION OF RECEIPT  
OF SEARCH COPY**

(PCT Rule 25.1)

Date of mailing  
(day/month/year)

11/09/2000

Applicant's or agent's file reference  
**X-12591**

**IMPORTANT NOTIFICATION**

International application No.  
**PCT/US 00/ 17864**

International filing date (day/month/year)

21/07/2000

Priority date (day/month/year)

29/07/1999

Applicant

**ELI LILLY AND COMPANY et al.**

**1. Where the International Searching Authority and the Receiving Office are not the same office:**

The applicant is hereby notified that the search copy of the international application was received by this International Searching Authority on the date indicated below.

**Where the International Searching Authority and the Receiving Office are the same office:**

The applicant is hereby notified that the search copy of the international application was received on the date indicated below.

23/08/2000 *(date of receipt).*

**2.  The search copy was accompanied by a nucleotide and/or amino acid sequence listing in computer readable form.**

**3. Time limit for establishment of International Search Report**

The applicant is informed that the time limit for establishing the International Search Report is 3 months from the date of receipt indicated above or 9 months from the priority date, whichever time limit expires later

**4. A copy of this notification has been sent to the International Bureau and, where the first sentence of paragraph 1 applies, to the Receiving Office.**

Name and mailing address of the International Searching Authority  
  
 European Patent Office, P.B. 5818 Patentlaan 2  
 NL-2280 HV Rijswijk  
 Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
 Fax: (+31-70) 340-3016

Authorized officer

**ISA/EP**

**PATENT COOPERATION TREATY**  
**PCT**  
**INTERNATIONAL PRELIMINARY EXAMINATION REPORT**  
**(PCT Article 36 and Rule 70)**

Applicant's or agent's file reference  X-12591	<b>FOR FURTHER ACTION</b>		See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No.  PCT/US00/17864	International filing date (day/month/year)  21/07/2000	Priority date (day/month/year)  29/07/1999	
International Patent Classification (IPC) or national classification and IPC C07D409/04			
Applicant  ELI LILLY AND COMPANY et al.			
<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 6 sheets, including this cover sheet.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of sheets.</p>			
<p>3. This report contains indications relating to the following items:</p> <ul style="list-style-type: none"> <li>I <input checked="" type="checkbox"/> Basis of the report</li> <li>II <input type="checkbox"/> Priority</li> <li>III <input checked="" type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</li> <li>IV <input type="checkbox"/> Lack of unity of invention</li> <li>V <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</li> <li>VI <input checked="" type="checkbox"/> Certain documents cited</li> <li>VII <input checked="" type="checkbox"/> Certain defects in the international application</li> <li>VIII <input type="checkbox"/> Certain observations on the international application</li> </ul>			
Date of submission of the demand  02/02/2001	Date of completion of this report  25.04.2001		
Name and mailing address of the international preliminary examining authority:   European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx. 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer   Rudolf, M  Telephone No. +49 89 2399 8604		

INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT

International application No. PCT/US00/17864

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):  
**Description, pages:**

1-76 as originally filed

**Claims, No.:**

1-6 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- the language of publication of the international application (under Rule 48.3(b)).
- the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- contained in the international application in written form.
- filed together with the international application in computer readable form.
- furnished subsequently to this Authority in written form.
- furnished subsequently to this Authority in computer readable form.
- The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- the description, pages:
- the claims, Nos.:
- the drawings, sheets:

5.  This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/US00/17864

*(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)*

6. Additional observations, if necessary:

**III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:
  - the entire international application.
  - claims Nos. 3-6.

because:

- the said international application, or the said claims Nos. 3-6 with respect to industrial applicability relate to the following subject matter which does not require an international preliminary examination (specify): see separate sheet
- the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (specify):
- the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- no international search report has been established for the said claims Nos. .

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:
  - the written form has not been furnished or does not comply with the standard.
  - the computer readable form has not been furnished or does not comply with the standard.

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Yes: Claims 1-6
	No: Claims
Inventive step (IS)	Yes: Claims 1-6
	No: Claims
Industrial applicability (IA)	Yes: Claims 1,2

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/US00/17864

No: Claims

2. Citations and explanations  
see separate sheet

**VI. Certain documents cited**

1. Certain published documents (Rule 70.10)

and / or

2. Non-written disclosures (Rule 70.9)

see separate sheet

**VII. Certain defects in the international application**

The following defects in the form or contents of the international application have been noted:  
see separate sheet

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/US00/17864

To section III:

Claims 3-6 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

To section V:

The relevant prior art is represented by the following documents cited in the search report:

- D1: US-A-5 436 246 (RONALD C. BERNOTAS) 25 July 1995 (1995-07-25)
- D2: PATENT ABSTRACTS OF JAPAN vol. 016, no. 071 (C-0913), 21 February 1992 (1992-02-21) & JP 03 264583 A (DAI ICHI SEIYAKU CO LTD), 25 November 1991 (1991-11-25)
- D3: EP-A-0 535 722 (DUPHAR INTERNATIONAL RESEARCH B.V.) 7 April 1993 (1993-04-07)
- D4: EP-A-0 398 413 (DUPHAR INTERNATIONAL RESEARCH B.V.) 22 November 1990 (1990-11-22)
- D5: EP-A-0 982 304 (ELI LILLY AND CO.) 1 March 2000 (2000-03-01)
- D6: WO 00 00196 A (ELI LILLY AND CO.) 6 January 2000 (2000-01-06)

The claimed subject matter is novel in view of the above-mentioned documents. The essential structural differences are: in view of the compounds in D1: the piperidine substituent instead of piperazine; D2: the piperidine-N is substituted by a group -A-Q which is heterocyclalkyl, whereas in the present compounds the piperidine-N is unsubstituted; D3,D4: 3-substituted piperidines vs. 4-substituted piperidines according to the present invention.

D1, D3, and D4 relate to serotonin-5HT1A and -D receptor agents. Closest prior art appears to be D2 which describes serotonin 2-receptor antagonists. In view of the

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/US00/17864

considerable structural differences between the presently claimed compounds and those disclosed in D2 (see the group -A-Q), it seems that the present compounds are not fairly suggested by D2. Therefore the claimed subject matter can be considered inventive over the cited prior art.

For the assessment of the present claims 3-6 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

**To section VI:**

Documents D5 (filing date 29.6.1999, published 1.3.2000, priority 30.6.1998) and D6 (filing date 29.6.1999, published 6.1.2000, priority 30.6.1998) disclose compounds which correspond to present formula (I), see D5, pages 24, 26, 27; D6 page 34. It appears that the compounds described in D5 and D6 have been excised from the scope of the present claims by means of the provisos.

**To section VII:**

The document D2 is considered as relevant prior art and therefore should be cited in the description (Rule 5.1.a)ii) PCT).

## PATENT COOPERATION TREATY

PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference <b>X-12591</b>	<b>FOR FURTHER ACTION</b> see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. <b>PCT/US 00/ 17864</b>	International filing date (day/month/year) <b>21/07/2000</b>	(Earliest) Priority Date (day/month/year) <b>29/07/1999</b>
Applicant <b>ELT LILLY AND COMPANY INC.</b>		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 4 sheets.

It is also accompanied by a copy of each prior art document cited in this report.

## 1. Basis of the report

a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

contained in the international application in written form.

filed together with the international application in computer readable form.

furnished subsequently to this Authority in written form.

furnished subsequently to this Authority in computer readable form.

the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2.  Certain claims were found unsearchable (See Box I).

### 3. Unity of invention is lacking (see Box II).

4. With regard to the title,

the text is approved as submitted by the applicant.  
 the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

the text is approved as submitted by the applicant.

the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the drawings to be published with the abstract is Figure No. 1.

- as suggested by the applicant.
- because the applicant failed to suggest a figure.
- because this figure better characterizes the invention.

None of the figures.

# INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/17864

**A. CLASSIFICATION OF SUBJECT MATTER**

IPC 7 C07D409/04 A61K31/4535 A61P25/24 A61P3/04

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07D A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

CHEM ABS Data

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 5 436 246 A (RONALD C. BERNOTAS) 25 July 1995 (1995-07-25) the whole document ---	1-6
Y	PATENT ABSTRACTS OF JAPAN vol. 016, no. 071 (C-0913), 21 February 1992 (1992-02-21) & JP 03 264583 A (DAI ICHI SEIYAKU CO LTD), 25 November 1991 (1991-11-25) abstract ---	1-6
Y	EP 0 535 722 A (DUPHAR INTERNATIONAL RESEARCH B.V.) 7 April 1993 (1993-04-07) the whole document ---	1-6 -/-

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

° Special categories of cited documents :

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \*&\* document member of the same patent family

Date of the actual completion of the international search

9 January 2001

Date of mailing of the international search report

17/01/2001

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Beslier, L

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/17864

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	EP 0 398 413 A (DUPHAR INTERNATIONAL RESEARCH B.V.) 22 November 1990 (1990-11-22) the whole document ---	1-6
P, Y	EP 0 982 304 A (ELI LILLY AND CO.) 1 March 2000 (2000-03-01) the whole document ---	1-6
P, Y	WO 00 00196 A (ELI LILLY AND CO.) 6 January 2000 (2000-01-06) the whole document ---	1-6
P, Y	WO 00 00303 A (ELI LILLY AND CO.) 6 January 2000 (2000-01-06) the whole document -----	1-6

**INTERNATIONAL SEARCH REPORT**

Information on patent family members

International Application No

PCT/US 00/17864

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
US 5436246	A 25-07-1995	AT 162190	T	15-01-1998
		AU 671494	B	29-08-1996
		AU 5132193	A	12-04-1994
		CA 2144947	A	31-03-1994
		DE 69316377	D	19-02-1998
		DE 69316377	T	27-08-1998
		EP 0660832	A	05-07-1995
		ES 2112434	T	01-04-1998
		FI 951249	A	16-03-1995
		GR 3026297	T	30-06-1998
		HU 72662	A	28-05-1996
		JP 8501559	T	20-02-1996
		KR 195809	B	15-06-1999
		NO 951015	A	15-05-1995
		NZ 256561	A	25-06-1996
		WO 9406789	A	31-03-1994
		DK 660832	T	14-09-1998
JP 03264583	A 25-11-1991	JP 2883995	B	19-04-1999
EP 535722	A 07-04-1993	AU 648185	B	14-04-1994
		AU 1955492	A	21-01-1993
		CA 2073643	A	16-01-1993
		CN 1070644	A, B	07-04-1993
		CZ 9202168	A	17-02-1993
		FI 923201	A	16-01-1993
		HU 62887	A	28-06-1993
		JP 5213943	A	24-08-1993
		NO 922732	A	18-01-1993
		NZ 243516	A	27-04-1994
		US 5409940	A	25-04-1995
		ZA 9205184	A	28-04-1993
EP 398413	A 22-11-1990	AU 625664	B	16-07-1992
		AU 5494490	A	22-11-1990
		CA 2016625	A	16-11-1990
		JP 3017058	A	25-01-1991
		NZ 233645	A	25-06-1992
		US 5296497	A	22-03-1994
		ZA 9003626	A	27-02-1991
EP 982304	A 01-03-2000	AU 4726699	A	17-01-2000
		WO 0000198	A	06-01-2000
WO 0000196	A 06-01-2000	AU 4850199	A	17-01-2000
WO 0000303	A 06-01-2000	US 6021791	A	08-02-2000
		DE 19928572	A	13-01-2000
		GB 2339071	A	12-01-2000
		US 6146468	A	14-11-2000